

Amendments to the Specification:

Please delete the paragraph at page 3, lines 6-16, beginning with "The present invention is directed to," and replace it with the following amended paragraph:

The present invention is directed to a bone growth composition which includes a substrate, bone growth protein, a source of calcium and a source of phosphate. The composition has an acidic buffering potential in physiological solution. In one embodiment, the composition further includes a biocompatible buffering agent to maintain the acidity of the composition. In further alternative embodiments, the sources of calcium and/or phosphate can be salts such as calcium monophosphate, calcium hydrogen phosphate, or calcium pyrophosphate. The substrate in the composition can be collagen, fibrin, alginate or mixtures thereof. The bone growth protein can be purified bone growth proteins, recombinantly produced bone growth protcins or mixtures thereof. In a preferred embodiment, the bone growth protein includes a purified bone growth protein composition known as Bone Protein.

Please delete the paragraph at page 15, line 21 and ending on page 16, line 5, beginning "Another process of the present invention ... , " and replace it with the following amended paragraph:

Another process of the present invention includes implanting a composition as broadly described above into a body for induction of bone growth. As noted above, most uses of the present invention are concerned with human applications. The process, however, is suitable for a wide variety of animals, particularly including other mammals. As used herein, the term "implanting" refers to placing the composition of the present invention in any bone defect or other area in which it is desired to have bone grow. By implanting the composition, bone formation is induced by the bone growth protein. Over time, preferred calcium and phosphate materials are resorbed allowing for uniform bone formation throughout a defect area.

Please delete the paragraph at page 15, lines 7-20, beginning with "If the dispersion was made ... , " and replace it with the following amended paragraph:

If the dispersion was made with a calcium salt, a phosphate salt is then added to the dispersion to heterogeneously precipitate a calcium phosphate salt directly onto the surface of the

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collagen fibrils. If the dispersion was made with a phosphate salt, a calcium salt is then added to the dispersion to heterogeneously precipitate a calcium phosphate salt directly onto the surface of the collagen fibrils. The interfacial adherence of the precipitate improves the mechanical rigidity and wettability of the composite sponges. The application of dehydrothermal collagen cross-linking techniques (e.g., 110°C, 24-72hrs, vacuum) are well known in the art. Such cross-linking techniques result in the formation of water stable, collagen sponges of superior physical properties. Such sponges can then be loaded with bone growth protein and used for induction of bone growth *in vivo*. In a preferred embodiment, the products are prepared by producing a 4% (by weight) collagen dispersion that contains solubilized calcium dichloride dihydrate ($\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$). A solution of disodium phosphate (Na_2HPO_4) is added to the heterogeneously precipitate calcium hydrogen phosphate dihydrate ($\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$) directly onto the surface of collagen fibrils.

Please delete the paragraph at page 16, line 11 and ending on page 17, line 2, beginning "In the case of hip replacement . . ." and replace it with the following amended paragraph:

In the case of hip replacement operations, the ball and socket joint of a hip is replaced when a person's hip is not functioning properly. The ball portion of a joint is replaced by surgical removal of the ball portion from the terminus of the femur. The artificial ball portion has a functional ball end with the opposite end being a spike which is inserted into the proximal end of the femur from which the natural ball portion was removed. The spike can have a porous surface so that bone growth around the spike can anchor the spike in the femur. The product of the present invention, in particulate form, is layered or packed between the spike and the cavity in the femur in which the spike is to be inserted. The socket portion of a joint is replaced by inserting an artificial socket into the natural socket. The artificial socket is sized to fit with the artificial ball. On the surface of the artificial socket which contacts the natural socket, the artificial socket can have a porous surface. The product of the present invention, in particulate form, is placed in the natural socket cavity so that upon placement of the artificial socket, the product is between the natural and artificial socket. In this manner, as bone is formed, the artificial socket is anchored in the natural socket.

Please delete the paragraph at page 20, lines 9-14, beginning with "In an inert screw cap container . . ." and replace it with the following amended paragraph:

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In an inert screw cap container, mix 600 mg of accepted Bovine tendon Type I collagen with 600 mg of either Ostite powder (NP) or devitalized ~~rat~~ bone matrix powder (NP). Add 14.4 g of acetic acid (1 vol%) to prepare gel dispersions containing 4 wt.% collagen. Stir with a spatula to homogenize the mixtures and to adequately wet the components. Vibrate the mixtures on a high intensity orbital shaker to remove trapped air bubbles. Allow mixtures to sit for at least 1 hour at room temperature.

Please delete the paragraph at page 20, line 24 and ending on page 21, line 7, beginning "Dilute a volume of BP . . ." and replace it with the following amended paragraph:

Dilute a volume of BP (produced as described in U.S. Patent No. 5,290,763) with a volume of 10mM HCl to prepare solutions of 10 mg BP/100 ml (15 ml) and 35 mg BP/100 ml (4.0 ml). In the Delrin loading plate, pipet 50 [ml] μ l of a solution on the top and bottom half of a collagen sponge (n=240 (10 mg), n=48 (35 mg)). Allow disks to stand in a chamber containing a moist paper towel (to prevent drying and sponge shrinkage) at ambient temperatures for 40-60 minutes. Cover the disk holding plate with Saran Wrap and place in a -80°C freezer for 40-60 min. Unwrap and carefully place in a freeze dryer flask. Freeze dry for a minimum of 12 hours then remove. The implant samples will respectively contain total BP masses of 10 and 35 [g] μ g.

Please delete the paragraph at page 21, lines 14-16, beginning with "The weight of each . . ." and replace it with the following amended paragraph:

The weight of each Long-Evans rat was recorded. Acceptable rats for bioassays weigh between 100 and 130g. The animals ~~was were~~ anesthetized with 400 ml of pentobarbital dosing solution injected i.p..

Please delete the paragraph at page 22, lines 5-10, beginning with "The testing protocol . . ." and replace it with the following amended paragraph:

The testing protocol involved subcutaneous implantation of collagen sponges (to assess endochondral bone formation) containing 10 [g] μ g BP. The samples were placed in four subcutaneous implantation sites: the upper quadrants of a rat's abdomen and dorsal thorax [Figure 1]